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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference L07892	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP00/00240	International filing date (day/month/year) 13 January 2000 (13.01.00)	Priority date (day/month/year) 14 January 1999 (14.01.99)
International Patent Classification (IPC) or national classification and IPC C07D 213/50, 213/57, 213/52		
Applicant LONZA AG		

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- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 6 sheets, including this cover sheet.
☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 5 sheets.

- This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 14 July 2000 (14.07.00)	Date of completion of this report 19 February 2001 (19.02.2001)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

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national application No.

PCT/EP00/00240

I. Basis of the report

1. This report has been drawn on the basis of *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*:

- ☒ the international application as originally filed.
- ☒ the description, pages 1-12, as originally filed,
 pages _____, filed with the demand,
 pages _____, filed with the letter of _____,
 pages _____, filed with the letter of _____.
- ☒ the claims, Nos. _____, as originally filed,
 Nos. _____, as amended under Article 19,
 Nos. _____, filed with the demand,
 Nos. 1-18, filed with the letter of 23 January 2001 (23.01.2001),
 Nos. _____, filed with the letter of _____.
- ☐ the drawings, sheets/fig _____, as originally filed,
 sheets/fig _____, filed with the demand,
 sheets/fig _____, filed with the letter of _____,
 sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1 - 18	YES
	Claims		NO
Inventive step (IS)	Claims	1 - 18	YES
	Claims		NO
Industrial applicability (IA)	Claims	1 - 18	YES
	Claims		NO

2. Citations and explanations

1. Reference is made to the international search report citations:

- D1: WO-A-99/15503
- D2: WO-A-99/55830
- D3: WO-A-98/47871
- D4: US-A-5 596 008
- D5: US-A-4 155 909
- D6: J. ORG. CHEM., 53(26), 1988, pages 6115-6118
- D7: BULL. SOC. CHIM. BELGES, 98(1), 1989,
pages 77 - 81
- D8: US-A-3 313 683
- D9: FR-A-2 074 674
- D10: 'Organic Chemistry' 1992 (XP002135946)
- D11: 'Pyridine and its Derivatives' 1964
(XP002135944)
- D12: 'Organic Chemistry' 1992 (XP002135945).

D1 and D2 were published between the priority date and filing date of the present application.

Therefore they are not considered prior art within the meaning of PCT Rule 64.1 and PCT Article 33(2) and (3) (see Box VI).

2. Novelty

a) The individual compound as per the current Claim 1 is covered by the scope of protection of Claim 20 of D3. The selection according to the application of R^1 when it means a methyl group combined with "Ar" as 5'-methyl-substituted 3-pyridinyl does not appear to be individualized in D3. Although methyl-substituted groups "Ar" are characterized as being preferred on page 8, line 15, and compounds of formula A2, in which R^1 is CH_3 , are mentioned by way of example in D3, the selection of R^1 and "Ar" according to the application does not appear to be disclosed. Therefore Claim 1 appears to meet the requirements of PCT Article 33(2).

b) The reaction of an N,N-dialkylamino-(6-methyl-3-pyridinyl)acetonitrile of formula III with a benzylhalide is not disclosed in the citations. The method as per Claim 2 (and of dependent claims, Claims 3 to 13) therefore appears to be novel within the meaning of PCT Article 33(2). Method Claim 18, which likewise includes these method features, can thus be considered novel within the meaning of the PCT.

c) The bisulphite adducts of formula I of D9 overlap with the structurally most similar compound II as per the current Claim 14. The compound produced in Example 23 of D9 differs from the adduct as per the application by the 3-pyridine group, which is not substituted in D9. Although alkyl-substituted groups are disclosed in general terms, the disclosure does not extend to methyl-substituted, that is, 6-methyl-

substituted pyridine groups. Therefore the subject matter of Claim 14 appears to be a novel selection from D9. Claim 15, which is directed to the method of production of this compound, therefore likewise appears to meet the requirements of PCT Article 33(2).

d) The compounds in Claim 16 overlap with the structurally most similar α -dimethylamino- α -pyridylacetonitrile derivatives of D8. Although column 2 contains "pyridyl or substituted pyridyl groups" and examples thereof, such as a "2-methylpyridyl group", for example (column 2, line 46), this citation does not appear to disclose the claimed combination of a 2-methylpyrid-3-yl group and an N,N-dialkyl group as the sole substituent of the acetonitrile. The claimed compounds therefore appear to concern a novel selection. Claim 16 and Claim 17, which is directed to a method of producing said compounds, therefore appear to meet the requirements of PCT Article 33(2).

3. Inventive step

The claimed subject matter as per the application concerns different intermediate products and methods of producing them.

a) The object of independent Claims 1, 2 and 18 is considered to be the devising of a method of producing (intermediate) compound I, which, according to page 1 of the description, is itself a starter product for producing pharmaceutical products.

Embodiments 4a and 4b substantiate the fact that said object is achieved by the technical features of Claim 2.

The proposed approach is via the reaction of a vinylpyridine derivative with ozone followed by reduction, the corresponding aldehyde or bisulphite addition compound II being formed. None of the citations appears to suggest this reaction method and so the overall method as per Claims 2 and 18, and the end product of the method as per Claim 1 appear to involve an inventive step pursuant to PCT Article 33(3).

b) The subject matter of Claim 14 concerns an intermediate product which is considered essential for the overall method, for the above reasons. As the applicant explained in the letter of 23 January 2001, this key product can, moreover, be produced in a single method step starting from the vinylpyridine compound, which is a considerable advantage over the prior art.

The intermediate product as per Claim 14 therefore appears to involve an inventive step. The method of producing it as per Claim 15, its further processing as per Claim 17 and the resultant novel intermediate product of formula III (Claim 16) therefore appear, as part of the inventive overall method and by their relation to the intermediate product as per Claim 14, to meet the requirements of PCT Article 33(3).

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: VI

1. D1 and D2 were published between the priority date and the filing date of the present application. Therefore they are not considered prior art within the meaning of PCT Rule 64.1 and PCT Article 33(2) and (3).

In the regional proceedings before the European Patent Office these documents will be used to assess novelty. It would appear that compounds 5a (D1) and PE-3 (D2) might be prejudicial to the novelty of Claim 1.